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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER	
TIDWELL, JUDY LILLE	

ART UNIT	PAPER NUMBER
1642	

DATE MAILED: 03/02/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/737,350	GEORGES ET AL.	
	Examiner	Art Unit	
	Judy Lille Tidwell, PhD	1642	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10/7/2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-108* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-108* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Restrictions

Restriction to one of the following inventions is required under 35 U.S.C. 121:

I. Claims 1-9, drawn to a method for detecting multidrug resistance or multidrug resistance potential in a test neoplastic cell comprising measuring a level of cell surface-expressed HSC70 protein in a test neoplastic cell and comparing this to the a nonresistant neoplastic cell, classified in class 435, subclass 7.21.

II. Claims 10-19, drawn to a method for detecting a multidrug resistant cell in a patient comprising administering a HSC70 binding agent and detecting said agent on a multidrug resistant cell in the patient, classified in class 435, subclass 4.

III. Claims 20, 22-27, 75-81, drawn to a kit for diagnosing or detecting multidrug resistance or neoplasia in a test neoplastic cell comprising a first probe for the detection of HSC70 and a second probe for the detection of a multidrug resistance marker or a neoplasia marker selected from the group consisting of nucleophosmin and HSC70, classified in class 435, subclass 810.

IV. Claims 21, 22-23, 26-28, drawn to a kit for diagnosing or detecting multidrug resistance in a test neoplastic cell comprising a first probe for the detection of HSC70 and a second probe for the detection of a multidrug resistance marker selected from the group consisting of MDR1, MDR3, MRP1, MRP5, LRP, classified in class 435, subclass 810.

V. Claims 29-31, drawn to a cell surface HSC70 *in situ* detection probe, classified in class 435, subclass 7.21.

VI. Claims 32-42, 82-92, drawn to a cell surface HSC70-targeted agent for treating or preventing a multidrug resistant neoplasm or a cancerous neoplastic cell growth, comprising a HSC70 binding component and a therapeutic component, classified in class 536, subclass 1.

VII. Claims 43-48, 93-98, drawn to a vaccine for treating or preventing a multidrug resistant neoplasm, comprising a HSC70 polypeptide, or subsequence thereof, and at least one pharmaceutically acceptable vaccine component, classified in class 530, subclass 387.1.

VIII. Claims 49-53, drawn to a method of treating or preventing a multidrug resistant neoplasm comprising administering a cell surface HSC70-targeted agent, classified in class 514, subclass 2.

IX. Claims 54-58, drawn to a method of treating or preventing a multidrug resistant neoplasm comprising administering a HSC70 vaccine, classified in class 424, subclass 193.1.

X. Claims 59-65, drawn to a method for detecting whether a test cell is neoplastic comprising measuring a level of cell surface-expressed HSC70 protein in a test cell and comparing this to a nonneoplastic cell, classified in class 435, subclass 7.21.

XI. Claims 66-74, drawn to a method for detecting a neoplastic cell in a patient comprising administering a HSC70 binding agent and detecting said agent on a neoplastic cell in the patient, classified in class 435, subclass 4.

XII. Claims 99-103, drawn to a method of treating or preventing a neoplasm comprising administering a cell surface HSC70-targeted therapeutic agent, classified in class 514, subclass 2.

XIII. Claims 104-108, drawn to a method of treating or preventing a neoplasm comprising administering a HSC70 vaccine, classified in class 424, subclass 193.1.

The inventions are distinct, each from the other because of the following reasons:

The inventions of Groups I, II, X, XI are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the specification does not disclose that their methods would be used together. The method of detecting multidrug resistance in a test neoplastic cell comprising measuring a level of cell surface-expressed HSC70 protein in a test neoplastic cell (Group I), a method for detecting a multidrug resistant cell in a patient comprising administering a HSC70 binding agent and detecting said agent (Group II), a method for detecting whether a test cell is neoplastic comprising measuring a level of cell surface-expressed HSC70 protein in a test cell (Group X), and a method for detecting a neoplastic cell in a patient comprising administering a HSC70 binding agent and detecting said agent (Group XI) are unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs this function using structurally and functionally divergent material. Moreover, the methodology and materials necessary for the detecting a multidrug resistanct or neoplastic cell by measuring protein expression or by using a binding agent differ significantly for each of the materials. For detecting any type of protein expression or agent in a test cell requires the use of separate and distinct cell types. For the detection of a property of a cell measuring protein expression, an antibody and a label may be used. For the detection of a property of a cell comprising administering a HSC70 binding agent and detecting said agent, the binding agent could be natural ligands, synthetic small molecules, chemicals, nucleic acids, peptides, proteins, or antibodies and the detectable labels could be fluorescence, radiation, chemoluminescence, or magnetic compounds. Therefore, each method is divergent in materials and steps. For these reasons the inventions of Groups I, II, X, XI are patentably distinct.

The inventions of Groups VIII, IX, XII, XIII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and

they have different modes of operation, different functions, or different effects (MPEP § 806.04, MPEP § 808.01). In the instant case the specification does not disclose that their methods would be used together. The method of treating or preventing a multidrug resistant neoplasm comprising administering a cell surface HSC70-targeted agent (Group VIII), a method of treating or preventing a multidrug resistant neoplasm comprising administering a HSC70 vaccine (Group IX), a method of treating or preventing a neoplasm comprising administering a cell surface HSC70-targeted therapeutic agent (Group XII), and a method of treating or preventing a neoplasm comprising administering a HSC70 vaccine (Group XIII) are unrelated as they comprise distinct steps and utilize different products which demonstrates that each method has a different mode of operation. Each invention performs this function using structurally and functionally divergent material. Moreover, the methodology and materials necessary for the detecting a multidrug resistanct or neoplastic cell by measuring protein expression or by using a binding agent differ significantly for each of the materials. For treating or preventing a neoplasm or a multidrug resistant neoplasm requires the use of separate and distinct cell types. For the method of treating or preventing a multidrug resistant neoplasm or a non-resistant neoplasm using a HSC70-targeted agent, any agent such as a small organic compound, peptide, antibody or inorganic compound may be used. For the method of treating or preventing a multidrug resistant neoplasm or a non-resistant neoplasm using a vaccine, a HSC70 polypeptide, or subsequence thereof, and a pharmaceutically acceptable carrier can be used. Therefore, each method is divergent in materials and steps. For these reasons the inventions of Groups VIII, IX, XII, XIII are patentably distinct.

The inventions of Groups III and IV are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case the different inventions are structurally and functionally distinct. While the inventions of Groups III and IV are both kits, in this instance the kit in Group III uses a first probe for the detection of HSC70 and a second probe for the detection of a multidrug resistance marker or a neoplasia marker selected from the group consisting of

nucleophosmin and HSC70 whereas the kit in Group IV uses a first probe for the detection of HSC70 and a second probe for the detection of a multidrug resistance marker selected from the group consisting of MDR1, MDR3, MRP1, MRP5, LRP. Each invention uses structurally and functionally divergent material. For these reasons the inventions of Groups III and IV are patentably distinct.

The inventions of Groups V, VI, and VII are unrelated. Inventions are unrelated if it can be shown that they are not disclosed as capable of use together and they have different designs, modes of operation, and effects (MPEP § 802.01 and § 806.06). In the instant case the different inventions are structurally and functionally distinct. The invention of Group V is drawn to an antibody used as a probe, Group VI is drawn to a HSC70-targeted agent, such as a small organic compound, peptide, antibody or inorganic compound, and Group VII is drawn to a vaccine comprising a HSC70 polypeptide, or subsequence thereof, and at least one pharmaceutically acceptable vaccine component. Each invention uses structurally and functionally divergent material. For these reasons the inventions of Groups V, VI, and VII are patentably distinct.

Inventions V and I, X are related as product and process of use. The inventions can be shown to be distinct if either or both of the following can be shown: (1) the process for using the product as claimed can be practiced with another materially different product or (2) the product as claimed can be used in a materially different process of using that product. See MPEP § 806.05(h). In the instant case invention V, a HSC70 detection probe, can be used in a materially different process than inventions I and X.

Species Election

Groups I-IV, VI-XIII contain claims directed to the following genuses of species of patentably distinct species of the claimed invention:

1. Neoplastic cells including a promyleocytic leukemia cell, a T lymphoblastoid cell, a breast epithelial cell, an ovarian cell, a lymphoma cell, a melanoma cell, a sarcoma cell, a leukemia cell, a retinoblastoma cell, a hepatoma cell, a myeloma cell, a glioma cell, a mesothelioma cell, and a carcinoma cell.

2. Tissues wherein the neoplastic cell is from including blood, bone marrow, spleen, lymph node, liver, thymus, kidney, brain, skin, gastrointestinal tract, eye, breast, prostate, and ovary.

3. Nonresistant neoplastic cell lines including HL60, N84, CEM, HSB2 Molt4, MCF-7, MDA, SKOV-3, and 2008.

4. HSC70 binding agents including an antibody or antibody fragments, Alzheimer's tau protein, BAG-I, small glutamine-rich tetratricopeptide repeat-containing protein (SGT), (aa 642-658) of rotavirus VP5 protein, auxilin, and the immunosuppressant s-deoxyspergualin (DSG), natural ligands, synthetic small molecules, chemicals, nucleic acids, peptides, proteins, and antibodies.

5. Detectable labels including fluorophores, chemical dyes, radioactive compounds, chemoluminescent compounds, magnetic compounds, parnmagnetic compounds, promagnetic compounds, enzymes that yield a colored product, enzymes that yield a chemoluminescent product, and enzymes that yield a magnetic product.

6. First probes for detection of HSC70 including an anti-HSC70 antibody, anti-HSC70 antibody fragment, and an HSC ligand such as Alzheimer's tau protein, BAG-I, small glutamine-rich tetratricopeptide repeat-containing protein (SGT), (aa 642-658) of rotavirus VP5 protein, auxilin, and the immunosuppressant s-deoxyspergualin (DSG).

7. Second probes for detection of a marker including HSC70, HSC70 antibody, MDR1, MDR3, MRP1, MRP5, and LRP, MDR1 antibody, MDR3 antibody, MRP1 antibody, MRP5 antibody, and LRP antibody, nucleophosmin, nucleophosmin antibody, nucleophosmin ligand, vimentin antibody, and vimentin ligand.

8. Therapeutic components including Actinomycin, Adriamycin, Altretnmine, Asparaginase, Bleomycin, Busulfan, Capecitabine, Carboplatin, Cnrmustine. Chlornmbucil, Cisplatin, Cladribine, Cyclophosphamide, Cytarabine, Dacarbazine, Dactinomycin, Daunorubicin, Docetaxel, Doxorubicin, Epoetin, Etoposide, Fludarabine,

Fluorouracil, Gemcitabine, Hydroxyurea, Idanlbicin, Ifosfamide, Imatinib, Irinotecan, Lomustine, Mechlorethamine, Melphalan, Mercaptopurine, Methotrexate, Mitomycin, Mitotane, Mitoxantrone, Paclitaxel, Pentostatin, Procarbazine, Taxol, Teniposide, Topotecan, Vinblastine, Vincristine, and Vinorelbine.

9. Radioisotopes including ^{90}Y, ^{125}I, ^{131}I, ^{211}At, and ^{213}Bi.

10. Toxins including Pseudomonas exotoxin, a diphtheria toxin, a plant ricin toxin, a plant abrin toxin, a plant saporin toxin, a plant gelonin toxin, and pokeweed antiviral protein.

11. Adjuvants including aluminum hydroxide, aluminum phosphate, calcium phosphate, oil emulsion, a bacterial product, whole inactivated bacteria, an endotoxins, cholesterol, a fatty acid, an aliphatic amine, a paraffinic compound, a vegetable oil, monophosphoryl lipid A, a saponin, and squalene.

12. Neoplasms including a breast cancer, an ovarian cancer, a myeloma, a lymphoma, a melanoma, a sarcoma, a leukernia, a retinoblastoma, a hepatoma, a glioma, a mesothelioma, and a carcinoma.

13. Tissues including blood, bone marrow, spleen, lymph node, liver, thymus, kidney, brain, skin, gastrointestinal tract, eye, breast, prostate, and ovary.

Group I contains 3 genuses of species; 1, 2, 3
Group II contains 5 genuses of species; 1, 2, 3, 4, 5
Group III contains 2 genuses of species; 6, 7
Group IV contains 2 genuses of species; 6, 7
Group VI contains 5 genuses of species; 4, 5, 8, 9, 10
Group VII contains 1 genus of species; 11
Group VIII contains 2 genuses of species; 12, 13
Group IX contains 2 genuses of species; 12, 13
Group X contains 2 genuses of species; 12, 13
Group XI contains 5 genuses of species; 1, 2, 3, 4, 5
Group XII contains 2 genuses of species; 12, 13
Group XIII contains 2 genuses of species; 12, 13

Accordingly, applicant must select one of each of the species within each genus. For example, if applicant elects Group I, one of each species of genuses 1, 2, and 3 must be selected. If applicant elects Group VI, one of each species of genuses 1, 2, 3, 4, and 5 must be selected.

In order to determine whether the Markush practice set forth in MPEP 803.02 must be followed, the office must assess whether members of each Markush group have unity of invention as defined by *In re Harnisch*, 631 F.2d 716, 206 USPQ 300(CCPA 1980); and *Ex parte Hozumi*, 3 USPQ2d 1059 (Bd. Pat. App. & Int. 1984). The appropriate test under Harnisch for unity of invention is whether members

1) share a common utility

2) share a substantial structural feature disclosed as being essential to that utility.

In the instant case, each of the genuses and species within each genus are structurally and functionally distinct assessed on the basis of their structure and their function, even though they may have the same utility. For example, in genuses of species 1-3, 12-13, neoplasms, neoplastic cells, the tissues from which they are derived, or cell lines are all distinct based on significantly different tissue- or cell-specific properties, characteristics, expression profiles, etc. In genuses of species 4-7, binding agents, labels, and probes are all distinct based on what they bind to (proteins, nucleic acids, antibodies, small molecules, etc.) and different detection properties (light, radiation, enzymatic reactions, magnetism, etc.). In genuses of species 8-11, therapeutic components, ratioisotopes, toxins, and adjuvants are all distinct based on significantly different chemical compositions.

Search Burden

The inventions of Groups I-XIII have separate status in the art as shown by their different classifications. Furthermore, the inventions have distinct steps and products that require separate and distinct searches. As such, it would be burdensome to search the inventions of Groups I-XIII.

Because these inventions are distinct for the reasons given above and have acquired a separate status in the art as shown by their different classification, restriction for examination purposes as indicated is proper. Furthermore, because these inventions are distinct for the reasons given above and the search of the literature required for one group is not required for another group, restriction for examination purposes as indicated is proper.

If Applicant elects any of Groups I-XIV, then Applicant is required under 35 U.S.C. 121 to elect a single disclosed species from each of the three genuses, for prosecution on the merits to which the claims shall be restricted if no generic claim is finally held to be allowable, even if this requirement is traversed.

Applicant is advised that a reply to this requirement must include an identification of the species that is elected consonant with this requirement, and a listing of all claims readable thereon, including any claims subsequently added. An argument that a claim is allowable or that all claims are generic is considered nonresponsive unless accompanied by an election.

Should applicant traverse on the ground that the species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C. 103(a) of the other invention.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the

rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103, and 112. Until an elected product claim is found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowed product claim will not be rejoined. See "Guidance on Treatment of Product and Process Claims in light of *In re Ochiai, In re Brouwer* and 35 U.S.C. § 103(b)," 1184 O.G. 86 (March 26, 1996). Additionally, in order to retain the right to rejoinder in accordance with the above policy, Applicant is advised that the process claims should be amended during prosecution either to maintain dependency on the product claims or to otherwise include the limitations of the product claims. **Failure to do so may result in a loss of the right to rejoinder.** Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Applicant is advised that the reply to this requirement to be complete must include an election of the invention to be examined even though the requirement be traversed (37 CFR 1.143).

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Judy Lille Tidwell, PhD whose telephone number is 571-272-5952. The examiner can normally be reached on 8:00AM - 5:00PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Jeffrey Siew can be reached on 571-272-0787. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

2-27-06

MISOOK YU
PRIMARY EXAMINER

JLT
Art Unit 1642